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=> s cartilage intermediated layer protein

L1 0 CARTILAGE INTERMEDIATED LAYER PROTEIN

=> s "CILP"

L2 44 "CILP"

=> dup remove l2

PROCESSING COMPLETED FOR L2

L3 14 DUP REMOVE L2 (30 DUPLICATES REMOVED)

=> s l3 and homolog

L4 1 L3 AND HOMOLOG

=> d l4 cbib abs

L4 ANSWER 1 OF 1 MEDLINE

1998389785 Document Number: 98389785. PubMed ID: 9722584. Cloning and deduced amino acid sequence of a novel cartilage protein (**CILP**) identifies a proform including a nucleotide pyrophosphohydrolase. Lorenzo P; Neame P; Sommarin Y; Heinegard D. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, P.O.Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23469-75. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The cDNA cloning and expression in vitro and in eukaryotic cells of a novel protein isolated from human articular cartilage, cartilage intermediate layer protein (**CILP**) is described. A single 4.2-kilobase mRNA detected in human articular cartilage encodes a polypeptide of 1184 amino acids with a calculated molecular mass of 132.5 kDa. The protein has a putative signal peptide of 21 amino acids, and is

a

proform of two polypeptides. The amino-terminal half corresponds to **CILP** (molecular mass of 78.5 kDa, not including post-translational modifications) and the carboxyl-terminal half corresponds to a protein homologous to a porcine nucleotide pyrophosphohydrolase, NTPPHase (molecular mass of 51.8 kDa, not including post-translational modifications). **CILP** has 30 cysteines and six putative N-glycosylation sites. The human **homolog** of porcine NTPPHase described here contains 10 cysteine residues and two putative N-glycosylation sites. In the precursor protein the NTPPHase region is immediately preceded by a tetrapeptide conforming to a furin proteinase cleavage consensus sequence. Expression of the full-length cDNA in a cell-free translation system and in COS-7 or EBNA cells indicates that

the

precursor protein is synthesized as a single polypeptide chain that is processed, possibly by a furin-like protease, into two polypeptides upon or preceding secretion.

=> d 13 1-14 cbib abs

L3 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2001 ACS

2001:397168 Document No. 135:16376 Assay of isomerized and/or optically inverted proteins and protein fragments. Christgau, Stephan; Henriksen, Dennis Bang; Cloos, Paul Andreas Compare (Osteometer Bio Tech A/s, Den.). PCT Int. Appl. WO 2001038872 A2 20010531, 46 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP11720 20001124. PRIORITY: GB 1999-28052 19991126.

AB A method of immuno-assay comprises immunol. measuring in a biol. sample the amt. of an isomerized or optically inverted non-collagen protein derived from cartilage or of one or more isomerized or optically inverted fragments from such a protein. The method may det. the amt. of at least one Asx or Glx contg. protein or protein fragment in said biol. sample, wherein Asx is .alpha.D Asp or Asn or is .beta.L or .beta.D Asp and Glx is .alpha.D Glu or Gln or .gamma.L or .gamma.D Glu. The protein may be aggrecan, CLP, COMP, or **CILP** or said fragment is a fragment of aggrecan, CLP, COMP, or **CILP**.

L3 ANSWER 2 OF 14 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1

2001151363 EMBASE Variations in site and levels of expression of chondrocyte nucleotide pyrophosphohydrolase with aging. Masuda I.; Iyama K.-I.; Halligan B.D.; Barbieri J.T.; Haas A.L.; McCarty D.J.; Ryan L.M.. Dr. I. Masuda, Division of Rheumatology, Department of Medicine, Medical College of Wisconsin, 9200 West Wisconsin Avenue, Milwaukee, WI 53226, United States. Journal of Bone and Mineral Research 16/5 (868-875) 2001. Refs: 34.

ISSN: 0884-0431. CODEN: JBMREJ. Pub. Country: United States. Language: English. Summary Language: English.

AB The aim of this study was to identify changes in cartilage intermediate layer protein/nucleotide pyrophosphohydrolase (**CILP**/NTPPH) expression in articular cartilage during aging. Adult (3-4 years old) and young (7-10 days old) porcine articular hyaline cartilage and fibrocartilage were studied by Northern blot analysis, in situ hybridization, and immunohistochemistry using a complementary DNA (cDNA) probe encoding porcine **CILP**/NTPPH and antibody to a synthetic peptide corresponding to a **CILP**/NTPPH sequence. Northern blot analysis of chondrocytes showed lower expression of **CILP**/NTPPH messenger RNA (mRNA) in young cartilage than in adult cartilage. In adult cartilage, extracellular matrix from the surface to the middeep zone was immunoreactive for **CILP**/NTPPH, especially in the pericellular matrix surrounding the middeep zone chondrocytes. In young cartilage, chondrocytes were moderately immunoreactive for **CILP**/NTPPH throughout all zones except the calcified zone. The matrix of young cartilage was negative except in the superficial zone. In young cartilage, **CILP**/NTPPH mRNA expression was undetectable. In adult cartilage, chondrocytes showed strong mRNA expression for **CILP**/NTPPH throughout middeep zones. Protein and mRNA signals were not detectable below the tidemark. **CILP**/NTPPH secretion into matrix around

chondrocytes increases with aging. In this extracellular site it may generate inorganic pyrophosphate and contribute to age-related calcium pyrophosphate dihydrate crystal deposition disease.

L3 ANSWER 3 OF 14 MEDLINE DUPLICATE 2
2001238133 Document Number: 21212516. PubMed ID: 11315923. Implication
of

cartilage intermediate layer protein in cartilage destruction in subsets of patients with osteoarthritis and rheumatoid arthritis. Tsuruha J; Masuko-Hongo K; Kato T; Sakata M; Nakamura H; Nishioka K. (St. Marianna University School of Medicine, Kawasaki, Japan.) ARTHRITIS AND RHEUMATISM, (2001 Apr) 44 (4) 838-45. Journal code: 90M; 0370605. ISSN: 0004-3591. Pub. country: United States. Language: English.

AB OBJECTIVE: To investigate whether cartilage intermediate layer protein (CILP), a protein recently cloned from human articular cartilage, is recognized as an autoantigen in patients with osteoarthritis (OA) and rheumatoid arthritis (RA), and whether the immune response against CILP is involved in disease pathogenesis. METHODS: Recombinant fusion proteins, which contain the first half (C1), second half (C2), or

3 fragments within the C2 region (designated C2F1, C2F2, and C2F3) of the non-porcine nucleotide pyrophosphohydrolase-homologous region of CILP, were prepared using Escherichia coli. Autoantibodies to these proteins in serum samples from patients with OA or RA and from age-matched healthy individuals were detected by enzyme-linked immunosorbent assay and Western blotting. In addition, mice were

immunized with a mixture of the C1 and C2 fusion proteins to assess the arthrogenicity of CILP. RESULTS: Production of antibodies to the C2 region was detected in 10.5% (11 of 105) of the tested OA patients and in 8.0% (7 of 88) of the tested RA patients, although antibodies to the

C1 region were rarely detected in either patient group. All C2F1, C2F2, and C2F3 fragments were found to carry autoepitopes. The C2F2 fusion protein was recognized most frequently in the tested OA patients, whereas the

C2F3 fusion protein was dominantly recognized in the tested RA patients. All 4 mice strains, DBA/1J, ICR, C57BL/6, and BALB/c, immunized with the CILP fusion proteins developed chronic arthritis; in particular, the ICR mice developed polyarthritis that was characterized by infiltration of mononuclear cells in the synovium and exfoliation of the surface of cartilage. CONCLUSION: The immune response to CILP may play a role in the pathogenesis of inflammatory joint destruction.

Our results support the role of an immune-mediated process in the joint destruction present in chronic arthropathies such as OA and RA. The results suggest that suppression of immune responses to various

components of the cartilage, such as CILP, might be therapeutically beneficial in these chronic arthropathies.

L3 ANSWER 4 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
2001:171719 Document No.: PREV200100171719. Development of pedotransfer functions for a profile cone penetrometer. Grunwald, S. (1); Rooney, D. J.; McSweeney, K.; Lowery, B.. (1) Earth Information Technologies Corporation, Madison, WI, 53714: grunwald@earthit.com, blowery@facstaff.wisc.edu USA. Geoderma, (March, 2001) Vol. 100, No. 1-2, pp. 25-47. print. ISSN: 0016-7061. Language: English. Summary Language: English.

AB In this study, we illustrate how profile cone penetrometers (PCP), can be used to measure penetration resistance rapidly to define zones similar in cone index (CI), which can be related to soil physical properties. The objective of this study was (i) to develop pedopedotransfer functions, which describe the relationship between CI and soil texture, bulk density

(rhob) and water content (theta), and (ii) to evaluate the sensitivity of parameters used in these functions. The data set represented soils formed in reworked silty loess overlying glacial till and/or lacustrine sediments. The global data set were grouped into subsets in terms of similar CIs. A horizontal hierarchical cluster analysis and a vertical point inflection method were used to derive cone index layer profiles (CILP1 to CILP5). Variability of CI within **CILPs** was small and variability of CI among **CILPs** was large. Within each group, CI was regressed with soil physical properties to develop pedotransfer functions. These were evaluated using the coefficient of determination (R^2). A sensitivity analysis was executed to evaluate the relative importance of different parameters in the regression models. For the

total

data set, R^2 ranged from 0.35 to 0.48. Pedotransfer functions for the **CILPs** showed largest R^2 with 0.62 for CILP1, 0.76 for CILP2, 0.70 for CILP3, 0.63 for CILP4 and 0.98 for CILP5. Depth, rhob, clay content and theta were variables with large predictive power. Textural variables had strong predictive power in the top layers, CILP1 and CILP2. In CILP4, clay contents along with rhob and theta were variables with large predictive power. In contrast, the predictive power of rhob and theta was strong in layers CILP3 and CILP5, whereas soil textural characteristics showed weak predictability of CI. Pedotransfer functions using the global data set showed large sensitivities for rhob and theta. Similar results were obtained for all other **CILPs**, except CILP4 where clay content showed a large sensitivity. Our results show that pedotransfer penetrometer data can improve our understanding of the spatial distribution of CI and soil physical properties at fine scale.

L3 ANSWER 5 OF 14 MEDLINE

DUPLICATE 4

2001079852 Document Number: 21017438. PubMed ID: 11145028. Expression of cartilage intermediate layer protein/nucleotide pyrophosphohydrolase parallels the production of extracellular inorganic pyrophosphate in response to growth factors and with aging. Hirose J; Masuda I; Ryan L M. (Department of Medicine, Medical College of Wisconsin, Milwaukee 53226, USA.) ARTHRITIS AND RHEUMATISM, (2000 Dec) 43 (12) 2703-11. Journal code: 90M. ISSN: 0004-3591. Pub. country: United States. Language: English.

AB OBJECTIVE: To evaluate the role of the extracellular inorganic pyrophosphate (ePpi)-generating ectoenzyme cartilage intermediate layer protein/nucleotide pyrophosphohydrolase (**CILP**/NTPPH) in chondrocyte Ppi elaboration, we studied **CILP**/NTPPH expression in response to growth factors during aging. METHODS: Porcine chondrocytes from adult (3-4-year-old) and young (2-week-old) animals were stimulated with transforming growth factor beta1 (TGFbeta1), which enhances ePpi elaboration, and/or insulin-like growth factor 1 (IGF-1), which diminishes

ePpi elaboration. Measurements of ePpi, NTPPH enzyme activity, Western blot analysis, reverse transcriptase-polymerase chain reaction (RT-PCR), and Northern blot analysis were performed. RESULTS: Elaboration of ePpi into conditioned media from adult chondrocytes was significantly increased

by TGFbeta1 and significantly inhibited by IGF-1, but no significant differences were observed in young chondrocytes. The protein levels of **CILP**/NTPPH by Western analysis in the media from adult and young porcine chondrocytes were increased by TGFbeta1. RT-PCR and Northern analysis showed that **CILP**/NTPPH messenger RNA (mRNA) expression in both adult and young chondrocytes was increased by TGFbeta1 and decreased by IGF-1, but these changes were less significant in the young chondrocytes. Basal and TGFbeta1-up-regulated levels of **CILP**/NTPPH expression were higher in adult chondrocytes than in young chondrocytes. CONCLUSION: These results provide evidence that **CILP**/NTPPH expression and ePpi elaboration are concomitantly stimulated by TGFbeta1 and down-regulated by IGF-1, especially in adult chondrocytes, implicating **CILP**/NTPPH as a functional participant in ePpi

elaboration. Increased **CILP**/NTPPH mRNA expression in chondrocytes derived from aged animals compared with young animals might promote the formation of calcium pyrophosphate dihydrate crystals in aged cartilage.

L3 ANSWER 6 OF 14 SCISEARCH COPYRIGHT 2001 ISI (R)

2000:948975 The Genuine Article (R) Number: 357JU. Difference of expression between cartilage intermediate layer protein/nucleotide pyrophosphohydrolase (**CILP**/NTPPH) and plasma cell membrane glycoprotein-1 (PC-1)/NTPPH in response to the growth factors and with aging.. Hirose J (Reprint); Masuda I; Ryan L M. ARTHRITIS AND

RHEUMATISM

(SEP 2000) Vol. 43, No. 9, Supp. [S], pp. 329-329. Publisher: LIPPINCOTT WILLIAMS & WILKINS. 530 WALNUT ST, PHILADELPHIA, PA 19106-3621. ISSN: 0004-3591. Language: English.

L3 ANSWER 7 OF 14 MEDLINE

DUPLICATE 5

1999452316 Document Number: 99452316. PubMed ID: 10524685. Exclusion of the gene for human cartilage intermediate layer protein in currently mapped calcium pyrophosphate dihydrate deposition syndromes. Marinescu R C; Nyce K; Serrano de la Pena L; Overhauser J; Williams C J. (Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.) ARTHRITIS AND RHEUMATISM, (1999 Oct) 42 (10) 2139-44. Journal code: 90M; 0370605. ISSN: 0004-3591. Pub. country: United States. Language: English.

AB OBJECTIVE: To map the gene for human cartilage intermediate layer protein (**CILP**) in order to assess its involvement in some familial forms of calcium pyrophosphate dihydrate (CPPD) deposition disease. METHODS: A radiation hybrid panel was analyzed for chromosomal assignment of the **CILP** gene within a 1-cM limit of resolution. The location of the gene for **CILP** was confirmed to reside at the observed radiation hybrid locus by fluorescence in situ hybridization. RESULTS: The human **CILP** gene resides at chromosome 15q21. CONCLUSION: This map location definitively excludes mutations in the **CILP** gene as the cause of certain familial forms of CPPD deposition disease that have been genetically mapped to chromosomes 8q and 5p.

L3 ANSWER 8 OF 14 MEDLINE

DUPLICATE 6

2000068039 Document Number: 20068039. PubMed ID: 10601732. The human **CILP** gene: exon/intron organization and chromosomal mapping. Lorenzo P; Aman P; Sommarin Y; Heinegard D. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, Sweden.) MATRIX BIOLOGY, (1999 Oct) 18 (5) 445-54. Journal code: B0T; 9432592. ISSN: 0945-053X. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The human cDNA for cartilage intermediate layer protein (**CILP**) codes for a larger precursor protein that consists of **CILP** and a homologue to porcine Nucleotide pyrophosphohydrolase (NTPPHase) [Lorenzo et al. 1998a. J. Biol. Chem. 273, 23469-23475]. The human gene has now been isolated and characterized. Southern blot analysis indicated a

single copy of the **CILP** gene in the human genome. The gene spans approximately 15.3 kbp of genomic DNA, and is organized in nine exons.

The 5' flanking region contains a putative promoter region with a TATA-like box localized from -29 to -23 bp upstream of the transcription start

site.

Analysis of the putative promoter region revealed potentially cis-regulatory eukaryotic elements such as GATA-1, MyoD, MZF1, and CdxA. The protein coding region begins in exon 2 with the putative signal peptide. **CILP** is encoded from exon 3 to exon 9. In addition, exon 9 also codes for the entire NTPPHase homologue and contains the 3' untranslated region of the gene. All the introns follow the 'gt-ag' rule, except the last intron, intron 8, that belongs to the minor class of pre-mRNA introns that contain 'at-ac' at their 5' and 3' ends,

respectively. The **CILP** gene was mapped to human chromosome 15q22.

L3 ANSWER 9 OF 14 MEDLINE DUPLICATE 7
1999253146 Document Number: 99253146. PubMed ID: 10319588. Genomic organization, mapping, and polymorphisms of the gene encoding human cartilage intermediate layer protein (**CILP**). Nakamura I; Okawa A; Ikegawa S; Takaoka K; Nakamura Y. (Laboratory of Molecular Medicine, University of Tokyo, Japan.) JOURNAL OF HUMAN GENETICS, (1999) 44 (3) 203-5. Journal code: CYJ; 9808008. ISSN: 1434-5161. Pub. country: Japan. Language: English.

AB The **CILP** gene encodes a proform of two polypeptides. One of them, cartilage intermediate layer protein (**CILP**), is a non-collagenous protein recently isolated from human articular cartilage. The other is homologous to a porcine nucleotide pyrophosphohydrolase (NTPPHase) whose enzymatic activity is highest in articular tissue. The investigation reported here revealed that the **CILP** gene consists of nine exons spanning approximately 15 kb of genomic DNA on chromosome 15q22. We also report six single nucleotide variations in this gene; five of them cause amino acid changes and the most common of them substitutes isoleucine for threonine at codon 395.

L3 ANSWER 10 OF 14 MEDLINE DUPLICATE 8
1998389785 Document Number: 98389785. PubMed ID: 9722584. Cloning and deduced amino acid sequence of a novel cartilage protein (**CILP**) identifies a proform including a nucleotide pyrophosphohydrolase. Lorenzo P; Neame P; Sommarin Y; Heinegard D. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, P.O.Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23469-75. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The cDNA cloning and expression in vitro and in eukaryotic cells of a novel protein isolated from human articular cartilage, cartilage intermediate layer protein (**CILP**) is described. A single 4.2-kilobase mRNA detected in human articular cartilage encodes a polypeptide of 1184 amino acids with a calculated molecular mass of 132.5 kDa. The protein has a putative signal peptide of 21 amino acids, and is

a

proform of two polypeptides. The amino-terminal half corresponds to **CILP** (molecular mass of 78.5 kDa, not including post-translational modifications) and the carboxyl-terminal half corresponds to a protein homologous to a porcine nucleotide pyrophosphohydrolase, NTPPHase (molecular mass of 51.8 kDa, not including post-translational modifications). **CILP** has 30 cysteines and six putative N-glycosylation sites. The human homolog of porcine NTPPHase described here contains 10 cysteine residues and two putative N-glycosylation

sites.

In the precursor protein the NTPPHase region is immediately preceded by a tetrapeptide conforming to a furin proteinase cleavage consensus sequence.

Expression of the full-length cDNA in a cell-free translation system and in COS-7 or EBNA cells indicates that the precursor protein is synthesized

as a single polypeptide chain that is processed, possibly by a furin-like protease, into two polypeptides upon or preceding secretion.

L3 ANSWER 11 OF 14 MEDLINE DUPLICATE 9
1998389784 Document Number: 98389784. PubMed ID: 9722583. A novel cartilage protein (**CILP**) present in the mid-zone of human articular cartilage increases with age. Lorenzo P; Bayliss M T; Heinegard D. (Department of Cell and Molecular Biology, University of Lund, P. O. Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23463-8. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB A novel, somewhat basic noncollagenous protein was purified from guanidine hydrochloride extracts of human articular cartilage using cesium chloride density gradient centrifugation, followed by ion-exchange chromatography at pH 5, and gel filtration on two serially coupled columns of Superose 6 and Superdex 200. The protein of 91.5 kDa contains a single polypeptide chain substituted with N-linked oligosaccharides. It appeared unique to cartilage as studied by enzyme-linked immunosorbent assay and immunoblots of various tissue extracts. Its concentration in articular cartilages showed some variability with age being lower in young individuals. It represents a chondrocyte product, since it is synthesized by articular chondrocytes in explant cultures. Interestingly, the distribution of the protein in the articular cartilage provides important information on the nature of chondrocytes at different compartments in the tissue. Thus, chondrocytes in the middle/deeper layers of the tissue in particular, appeared to have produced the protein and deposited it in the interterritorial matrix. The protein was neither seen in the superficial nor in the deepest regions of the articular cartilage. Based on its immunolocalization we have named this protein **CILP** (cartilage intermediate layer protein).

L3 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2001 ACS

1996:450891 Amygdala activity at encoding correlated with long-term, free recall of emotional information. Cahill, Larry; Haier, Richard J.; Fallon, James; Alkire, Michael T.; Tang, Cheuk; Keator, David; Wu, Joseph;

McGaugh, James L. (Center Neurobiology Learning Memory, University California, Irvine, CA, 92697-3800, USA). Proc. Natl. Acad. Sci. U. S. A., 93(15), 8016-8021 (English) 1996. CODEN: PNASA6. ISSN: 0027-8424.

AB Positron emission tomog. of cerebral glucose metab. in adult human subjects was used to investigate amygdaloid complex (AC) activity assocd. with the storage of long-term memory for emotionally arousing events. Subjects viewed two videos (one in each of two sep. positron emission tomog. sessions, sepd. by 3-7 days) consisting either of 12 emotionally arousing film clips ("E cilp session) or of 12 relatively emotionally neutral film clips ("N" film session), and rated their emotional reaction to each film clip immediately after viewing it. Three weeks after the second session, memory for the videos was assessed in a free recall test. As expected, the subjects' av. emotional reaction to the E films was higher than that for the N films. In addn., the subjects recalled significantly more E films than N films. Glucose metabolic rate of the right AC while viewing the E films was highly correlated with the no. of E films recalled. AC activity was not significantly correlated with the no. of N films recalled. The findings support the view derived from both animal and human investigations that the AC is selectively involved with the formation of enhanced long-term memory assocd. with emotionally arousing events.

L3 ANSWER 13 OF 14 MEDLINE

93191471 Document Number: 93191471. PubMed ID: 8447680. An asymptomatic penile lesion. Circular indurated lymphangitis of the penis (**CILP**) with concurrent syphilis. Leventhal L C; Jaworsky C; Werth V. (Philadelphia Veterans Affairs Medical Center, Pa.) ARCHIVES OF DERMATOLOGY, (1993 Mar) 129 (3) 366-7, 369-70. Journal code: 6WU; 0372433. ISSN: 0003-987X. Pub. country: United States. Language: English.

L3 ANSWER 14 OF 14 SCISEARCH COPYRIGHT 2001 ISI (R)

93:175009 The Genuine Article (R) Number: KR036. AN ASYMPTOMATIC PENILE LESION - CIRCULAR INDURATED LYMPHANGITIS OF THE PENIS (**CILP**) WITH CONCURRENT SYPHILIS. LEVENTHAL L C (Reprint); JAWORSKY C; WERTH V. VET AFFAIRS MED CTR, PHILADELPHIA, PA, 19104 (Reprint). ARCHIVES OF DERMATOLOGY (MAR 1993) Vol. 129, No. 3, pp. 366. ISSN: 0003-987X. Pub. country: USA. Language: ENGLISH.

=> s cartilage

L5 144746 CARTILAGE

=> s 15 and intermediate

L6 1832 L5 AND INTERMEDIATE

=> s 16 and layer

L7 315 L6 AND LAYER

=> s 17 and protein

L8 102 L7 AND PROTEIN

=> s 18 and peptide

L9 22 L8 AND PEPTIDE

=> s 19 and dog

L10 0 L9 AND DOG

=> s 19 and cat

L11 0 L9 AND CAT

=> dup remove 19

PROCESSING COMPLETED FOR L9

L12 8 DUP REMOVE L9 (14 DUPLICATES REMOVED)

=> d l12 1-8 cbib abs

L12 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2001 ACS

2001:397168 Document No. 135:16376 Assay of isomerized and/or optically inverted **proteins** and **protein** fragments. Christgau, Stephan; Henriksen, Dennis Bang; Cloos, Paul Andreas Compare (Osteometer Bio Tech A/s, Den.). PCT Int. Appl. WO 2001038872 A2 20010531, 46 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY,

BZ,

CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP11720 20001124. PRIORITY: GB 1999-28052 19991126.

AB A method of immuno-assay comprises immunol. measuring in a biol. sample the amt. of an isomerized or optically inverted non-collagen **protein** derived from **cartilage** or of one or more isomerized or optically inverted fragments from such a **protein**. The method may det. the amt. of at least one Asx or Glx contg. **protein** or **protein** fragment in said biol. sample, wherein Asx is .alpha.D Asp or Asn or is .beta.L or .beta.D Asp and Glx is

.alpha.D Glu or Gln or .gamma.L or .gamma.D Glu. The **protein** may be aggrecan, CLP, COMP, or CILP or said fragment is a fragment of aggrecan, CLP, COMP, or CILP.

2001:483536 The Genuine Article (R) Number: 439UC. Molecular patterning of the oikoplastic epithelium of the larvacean tunicate *Oikopleura dioica*. Spada F; Steen H; Troedsson C; Kallesoe T; Spriet E; Mann M; Thompson E M (Reprint). Bergen High Technol Ctr, Sars Int Ctr Marine Mol Biol, N-5008 Bergen, Norway (Reprint); Univ So Denmark Odense, Dept Biochem & Mol Biol,

Prot Interact Lab, DK-5230 Odense, Denmark. JOURNAL OF BIOLOGICAL CHEMISTRY (8 JUN 2001) Vol. 276, No. 23, pp. 20624-20632. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. ISSN: 0021-9258. Pub. country: Norway; Denmark. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Appendicularia are protochordates that rely on a complex mucous secretion, the house, to filter food particles from seawater. A monolayer of cells covering the trunk of the animal, the oikoplastic epithelium, secretes the house. This epithelium contains a fixed number of cells arranged in characteristic patterns with distinct sizes and nuclear morphologies. Certain house structures appear to be spatially related to defined, underlying groups of cells in the epithelium. We show that the house is composed of at least 20 polypeptides, a number of which are highly glycosylated, with glycosidase treatments resulting in molecular mass shifts exceeding 100 kDa. Nano electrospray tandem mass spectrometric microsequencing of house polypeptides was used to design oligonucleotides to screen an adult *Oikopleura dioica* cDNA library. This resulted in the isolation of cDNAs coding for three different **proteins**, oikosin 1, oikosin 2, and oikosin 3. The latter two are novel **proteins** unrelated to any known data base entries. Oikosin 1 has 13 repeats of a Cys domain, previously identified as a subunit of repeating sequences in some vertebrate mucins. We also find one repeat of this Cys domain in human **cartilage intermediate layer protein** but find no evidence of this domain in any invertebrate species, including those for which entire genomes have been sequenced,

The three oikosins show distinct and complementary expression patterns restricted to the oikoplastic epithelium. This easily accessible epithelium, with differential gene expression patterns in readily identifiable groups of cells with distinctive nuclear morphologies, is a highly attractive model system for molecular studies of pattern formation.

2001151363 EMBASE Variations in site and levels of expression of chondrocyte nucleotide pyrophosphohydrolase with aging. Masuda I.; Iyama K.-I.; Halligan B.D.; Barbieri J.T.; Haas A.L.; McCarty D.J.; Ryan L.M.. Dr. I. Masuda, Division of Rheumatology, Department of Medicine, Medical College of Wisconsin, 9200 West Wisconsin Avenue, Milwaukee, WI 53226, United States. Journal of Bone and Mineral Research 16/5 (868-875) 2001. Refs: 34.

ISSN: 0884-0431. CODEN: JBMREJ. Pub. Country: United States. Language: English. Summary Language: English.

AB The aim of this study was to identify changes in **cartilage intermediate layer protein/nucleotide pyrophosphohydrolase (CILP/NTPPH)** expression in articular **cartilage** during aging. Adult (3-4 years old) and young (7-10 days old) porcine articular hyaline **cartilage** and fibrocartilage were studied by Northern blot analysis, in situ hybridization, and immunohistochemistry using a complementary DNA (cDNA) probe encoding porcine CILP/NTPPH and antibody to a synthetic **peptide** corresponding to a CILP/NTPPH sequence. Northern blot analysis of chondrocytes showed lower expression of CILP/NTPPH messenger RNA (mRNA)

in young **cartilage** than in adult **cartilage**. In adult **cartilage**, extracellular matrix from the surface to the middeep

zone was immunoreactive for CILP/NTPPH, especially in the pericellular matrix surrounding the middeep zone chondrocytes. In young **cartilage**, chondrocytes were moderately immunoreactive for CILP/NTPPH throughout all zones except the calcified zone. The matrix of young **cartilage** was negative except in the superficial zone. In young **cartilage**, CILP/NTPPH mRNA expression was undetectable. In adult **cartilage**, chondrocytes showed strong mRNA expression for CILP/NTPPH throughout middeep zones. **Protein** and mRNA signals were not detectable below the tidemark. CILP/NTPPH secretion into matrix around chondrocytes increases with aging. In this extracellular site it may generate inorganic pyrophosphate and contribute to age-related calcium pyrophosphate dihydrate crystal deposition disease.

L12 ANSWER 4 OF 8 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:692582 The Genuine Article (R) Number: 233FM. Noncollagenous, nonproteoglycan macromolecules of **cartilage**. Neame P J (Reprint); Tapp H; Azizan A. UNIV S FLORIDA, COLL MED, DEPT BIOCHEM & MOL BIOL, BOX 7, 12901 BRUCE B DOWNS BLVD, TAMPA, FL 33612 (Reprint); UNIV S FLORIDA, INST BIOMOL SCI, TAMPA, FL 33612; SHRINERS HOSP CRIPPLED CHILDREN, TAMPA, FL 33612. CELLULAR AND MOLECULAR LIFE SCIENCES (15 AUG 1999) Vol. 55, No. 10, pp. 1327-1340. Publisher: BIRKHAUSER VERLAG AG. VIADUKSTRASSE 40-44, PO BOX 133, CH-4010 BASEL, SWITZERLAND. ISSN: 1420-682X. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Extracellular matrix comprises approximately 90% of **cartilage**, with collagens and proteoglycans making up the bulk of the tissue. In recent years, several abundant **cartilage proteins** that are neither collagens nor proteoglycans have been characterized in detail.

The putative roles of these **proteins** range from involvement in matrix organization or matrix-cell signaling (PRELP, chondroadherin, **cartilage oligomeric protein** and **cartilage matrix protein**) through to molecules that are likely to be involved with modulation of the chondrocyte phenotype (CD-RAP, CDMPs, chondromodulin and pleiotrophin). Other molecules, such as the **cartilage-derived C-type lectin** and **cartilage intermediate layer protein** have no role as yet. Due to the difficulties associated with experimentally manipulating

a tissue that is 90% extracellular matrix in a manner that can be readily transferred to the whole organism, many of these molecules have been focused on by a surprisingly small number of researchers. This review focuses on newly discovered **proteins** and glycoproteins in **cartilage**, with a bias towards those that have structural roles or that are unique to **cartilage**.

L12 ANSWER 5 OF 8 MEDLINE DUPLICATE 2
2000068039 Document Number: 20068039. PubMed ID: 10601732. The human CILP

gene: exon/intron organization and chromosomal mapping. Lorenzo P; Aman P; Sommarin Y; Heinegard D. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, Sweden.) MATRIX BIOLOGY, (1999 Oct) 18 (5) 445-54. Journal code: BOT; 9432592. ISSN: 0945-053X. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The human cDNA for **cartilage intermediate layer protein** (CILP) codes for a larger precursor **protein** that consists of CILP and a homologue to porcine Nucleotide pyrophosphohydrolase (NTPPHase) [Lorenzo et al. 1998a. J. Biol. Chem. 273, 23469-23475]. The human gene has now been isolated and characterized. Southern blot analysis indicated a single copy of the CILP

gene in the human genome. The gene spans approximately 15.3 kbp of genomic DNA, and is organized in nine exons. The 5' flanking region contains a putative promoter region with a TATA-like box localized from -29 to -23 bp upstream of the transcription start site. Analysis of the putative promoter region revealed potentially cis-regulatory eukaryotic elements such as GATA-1, MyoD, MZF1, and CdxA. The **protein** coding region begins in exon 2 with the putative signal **peptide**. CILP is encoded from exon 3 to exon 9. In addition, exon 9 also codes for the entire NTPPHase homologue and contains the 3' untranslated region of the gene. All the introns follow the 'gt-ag' rule, except the last intron, intron 8, that belongs to the minor class of pre-mRNA introns that contain 'at-ac' at their 5' and 3' ends, respectively. The CILP gene was mapped to human chromosome 15q22.

L12 ANSWER 6 OF 8 MEDLINE DUPLICATE 3
 1998389785 Document Number: 98389785. PubMed ID: 9722584. Cloning and deduced amino acid sequence of a novel **cartilage protein** (CILP) identifies a proform including a nucleotide pyrophosphohydrolase. Lorenzo P; Neame P; Sommarin Y; Heinegard D. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, P.O.Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23469-75. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The cDNA cloning and expression in vitro and in eukaryotic cells of a novel **protein** isolated from human articular **cartilage**, **cartilage intermediate layer protein** (CILP) is described. A single 4.2-kilobase mRNA detected in human articular **cartilage** encodes a polypeptide of 1184 amino acids with a calculated molecular mass of 132.5 kDa. The **protein** has a putative signal **peptide** of 21 amino acids, and is a proform of two polypeptides. The amino-terminal half corresponds to CILP (molecular mass of 78.5 kDa, not including post-translational modifications) and the carboxyl-terminal half corresponds to a **protein** homologous to a porcine nucleotide pyrophosphohydrolase, NTPPHase (molecular mass of 51.8 kDa, not including post-translational modifications). CILP has 30 cysteines and six putative N-glycosylation sites. The human homolog of porcine NTPPHase described here contains 10 cysteine residues and two putative N-glycosylation sites. In the precursor **protein** the NTPPHase region is immediately preceded by a tetrapeptide conforming to a furin proteinase cleavage consensus sequence. Expression of the full-length cDNA in a cell-free translation system and in COS-7 or EBNA cells indicates that the precursor **protein** is synthesized as a single polypeptide chain that is processed, possibly by a furin-like protease, into two polypeptides upon or preceding secretion.

L12 ANSWER 7 OF 8 MEDLINE
 1998389784 Document Number: 98389784. PubMed ID: 9722583. A novel **cartilage protein** (CILP) present in the mid-zone of human articular **cartilage** increases with age. Lorenzo P; Bayliss M T; Heinegard D. (Department of Cell and Molecular Biology, University of Lund, P. O. Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23463-8. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB A novel, somewhat basic noncollagenous **protein** was purified from guanidine hydrochloride extracts of human articular **cartilage** using cesium chloride density gradient centrifugation, followed by ion-exchange chromatography at pH 5, and gel filtration on two serially coupled columns of Superose 6 and Superdex 200. The **protein** of 91.5 kDa contains a single polypeptide chain substituted with N-linked

oligosaccharides. It appeared unique to **cartilage** as studied by enzyme-linked immunosorbent assay and immunoblots of various tissue extracts. Its concentration in articular **cartilages** showed some variability with age being lower in young individuals. It represents a chondrocyte product, since it is synthesized by articular chondrocytes in explant cultures. Interestingly, the distribution of the **protein** in the articular **cartilage** provides important information on the nature of chondrocytes at different compartments in the tissue. Thus, chondrocytes in the middle/deeper **layers** of the tissue in particular, appeared to have produced the **protein** and deposited it in the interterritorial matrix. The **protein** was neither seen in the superficial nor in the deepest regions of the articular **cartilage**. Based on its immunolocalization we have named this **protein CILP (cartilage intermediate layer protein)**.

L12 ANSWER 8 OF 8 MEDLINE DUPLICATE 4
 90368670 Document Number: 90368670. PubMed ID: 2394708. Bone acidic glycoprotein-75 is a major synthetic product of osteoblastic cells and localized as 75- and/or 50-kDa forms in mineralized phases of bone and growth plate and in serum. Gorski J P; Griffin D; Dudley G; Stanford C; Thomas R; Huang C; Lai E; Karr B; Solursh M. (Division of Molecular Biology and Biochemistry, School of Basic Life Sciences, University of Missouri, Kansas City 64110.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1990 Sep 5) 265 (25) 14956-63. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Anti-**peptide** and anti-**protein** antisera were produced which both recognize bone acidic glycoprotein-75 (Mr = 75,000) and an apparent fragment or biosynthetic **intermediate** (Mr = 50,000) in calcified tissues and/or serum. A fragment-precursor relationship is suggested from the fact that closely spaced doublet polypeptides of Mr = 50,000 could be produced by proteolysis of the purified **protein** upon long term storage. No reactivity was detected with osteopontin, bone sialoprotein, or small bone proteoglycans. Bone acidic glycoprotein-75 represents 0.5-1% of the total radiolabeled **proteins** synthesized by explant cultures of neonatal calvaria or growth plate, by calvarial outgrowth cultures, and by rat osteosarcoma cells. Amounts produced by explant cultures and calvarial outgrowth cultures were similar to that for osteopontin, a major product of osteoblasts. In osteosarcoma cultures, 80% of labeled antigens were associated with the cell **layer** fraction wherein specific immunoprecipitation pelleted Mr = 50,000 and 75,000 sized antigens. Bone acidic glycoprotein-75 (Mr = 75,000) is enriched in 4 M guanidine HCl/0.5 EDTA extracts of neonatal rat bone and growth plate tissues, whereas largely absent from heart, lung, spleen, liver, brain, and kidney. Explant cultures of these noncalcifying tissues also synthesized bone acidic glycoprotein-75 antigen, but the quantities produced were only 5% or less that obtained with calvaria. By immunohistochemistry, antigenicity is associated with the bony shaft and calcified **cartilage** of long bones, but is absent from associated soft tissues. These finding demonstrate that bone acidic glycoprotein-75 is antigenically distinct, predominantly localized to calcified tissues, represents a major product of normal osteoblastic cells and may undergo a characteristic fragmentation in vivo and in vitro.

=> s heinegard d?/au or lorenzo p?/au

L13 1700 HEINEGARD D?/AU OR LORENZO P?/AU

=> s l13 and "CILP"

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PROCESSING COMPLETED FOR L14

L15 3 DUP REMOVE L14 (12 DUPLICATES REMOVED)

=> d l15 1-3 cbib abs

L15 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
 2000068039 Document Number: 20068039. PubMed ID: 10601732. The human **CILP** gene: exon/intron organization and chromosomal mapping. **Lorenzo P**; Aman P; Sommarin Y; **Heinegard D**. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, Sweden.) **MATRIX BIOLOGY**, (1999 Oct) 18 (5) 445-54. Journal code: BOT; 9432592. ISSN: 0945-053X. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

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L15 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
 1998389785 Document Number: 98389785. PubMed ID: 9722584. Cloning and deduced amino acid sequence of a novel cartilage protein (**CILP**) identifies a proform including a nucleotide pyrophosphohydrolase. **Lorenzo P**; Neame P; Sommarin Y; **Heinegard D**. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, P.O.Box 94, S-221 00 Lund, Sweden.) **JOURNAL OF BIOLOGICAL CHEMISTRY**, (1998 Sep 4) 273 (36) 23469-75. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The cDNA cloning and expression in vitro and in eukaryotic cells of a novel protein isolated from human articular cartilage, cartilage intermediate layer protein (**CILP**) is described. A single 4.2-kilobase mRNA detected in human articular cartilage encodes a polypeptide of 1184 amino acids with a calculated molecular mass of 132.5 kDa. The protein has a putative signal peptide of 21 amino acids, and is a proform of two polypeptides. The amino-terminal half corresponds to **CILP** (molecular mass of 78.5 kDa, not including post-translational modifications) and the carboxyl-terminal half corresponds to a protein homologous to a porcine nucleotide pyrophosphohydrolase, NTPPHase (molecular mass of 51.8 kDa, not including post-translational modifications). **CILP** has 30 cysteines and six putative

N-glycosylation sites. The human homolog of porcine NTPPHase described here contains 10 cysteine residues and two putative N-glycosylation sites.

In the precursor protein the NTPPHase region is immediately preceded by a tetrapeptide conforming to a furin proteinase cleavage consensus sequence.

Expression of the full-length cDNA in a cell-free translation system and in COS-7 or EBNA cells indicates that the precursor protein is synthesized

as a single polypeptide chain that is processed, possibly by a furin-like protease, into two polypeptides upon or preceding secretion.

L15 ANSWER 3 OF 3 MEDLINE DUPLICATE 3
1998389784 Document Number: 98389784. PubMed ID: 9722583. A novel cartilage protein (CILP) present in the mid-zone of human articular cartilage increases with age. **Lorenzo P**; Bayliss M T; **Heinegard D**. (Department of Cell and Molecular Biology, University of Lund, P. O. Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23463-8. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

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(FILE 'HOME' ENTERED AT 13:05:27 ON 09 OCT 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:05:43 ON 09 OCT 2001

L1 0 S CARTILAGE INTERMEDIATED LAYER PROTEIN
L2 44 S "CILP"
L3 14 DUP REMOVE L2 (30 DUPLICATES REMOVED)
L4 1 S L3 AND HOMOLOG
L5 144746 S CARTILAGE
L6 1832 S L5 AND INTERMEDIATE
L7 315 S L6 AND LAYER
L8 102 S L7 AND PROTEIN
L9 22 S L8 AND PEPTIDE
L10 0 S L9 AND DOG
L11 0 S L9 AND CAT
L12 8 DUP REMOVE L9 (14 DUPLICATES REMOVED)
L13 1700 S HEINEGARD D?/AU OR LORENZO P?/AU
L14 15 S L13 AND "CILP"
L15 3 DUP REMOVE L14 (12 DUPLICATES REMOVED)

=> s l3 and hog

L16 0 L3 AND HOG

=> s l3 and dog

L17 0 L3 AND DOG

=> s l3 and cat

L18 0 L3 AND CAT

=> s l3 and homolog

L19 1 L3 AND HOMOLOG

=> d l19 cbib abs

L19 ANSWER 1 OF 1 MEDLINE

1998389785 Document Number: 98389785. PubMed ID: 9722584. Cloning and deduced amino acid sequence of a novel cartilage protein (**CILP**) identifies a proform including a nucleotide pyrophosphohydrolase. Lorenzo P; Neame P; Sommarin Y; Heinegard D. (Department of Cell and Molecular Biology, Section for Connective Tissue Biology, University of Lund, P.O.Box 94, S-221 00 Lund, Sweden.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23469-75. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

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the precursor protein is synthesized as a single polypeptide chain that is processed, possibly by a furin-like protease, into two polypeptides upon or preceding secretion.

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n